The rejection of claims 8-10, 12 and 13 under 35 U.S.C. 112, second paragraph, is respectfully traversed. Claims 12 and 13 were canceled in the Preliminary Amendment dated July 30, 2001. With respect to claims 8-10, although applicants do not agree with the rejection, it is respectfully submitted that the rejection has been rendered moot by the amendments to the claims.

The rejection of claims 1-3 under 35 U.S.C. 102(b) as being anticipated by Chang (US 4,405,357) is respectfully traversed for the reasons set forth below.

The Chang patent does not teach isoxazole herbicides. Instead, the Chang patent teaches isoxazolidinone herbicides. Isoxazole herbicides and isoxazolidinone herbicides belong to two separate classes of herbicides. They are structurally distinct and act on different biochemical targets. For the convenience of the Examiner, applicants have enclosed extracts from the pesticide manual (electronic version, version 2.1 - Ed. CDS Tomlin) for clomazone, an isoxazolidinone herbicide, and isoxaflutole, an isoxazole herbicide. Accordingly, in view of the above, it is respectfully submitted that present claims 1-3 are not anticipated by the Chang patent.

The rejection of claims 4-6 and 11 under 35 U.S.C. 103(a), as being unpatentable over the Chang patent, is respectfully traversed for the reasons set forth above concerning the rejection under 35 U.S.C. 102. Specifically, the teachings of the Chang patent relate to a different class of herbicides with different properties. In addition, Chang does not describe or suggest the problems of herbicidal efficacy encountered during the application of isoxazole herbicides, for example the breakdown of the isoxazole herbicide to form the diketonitrile (DKN) and the subsequent mobility of the DKN following rainfall. Accordingly, since the Chang patent does not teach or suggest isoxazole herbicides or the problems associated with using isoxazole herbicides, the reference cannot teach or render obvious a method of overcoming those problems, such as the method that is claimed in the present patent application.

In view of the above remarks, it is respectfully submitted that the claims of the present patent application are not obvious in view of the Chang patent.

Withdrawal of the rejections under 35 U.S.C. 102, 103 and 112, and the allowance of claims 1-11 and 14-22, is respectfully requested.

Respectfully submitted,
CONNOLLY BOVE LODGE & HUTZ LLP

By _____
William E. McShane
Registration No. 32,707
Telephone: 302/658-9141

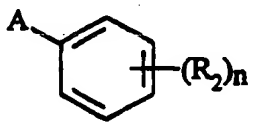
Enclosures: Appendix A
Copies of extracts for clomazone and isoxaflutole
Submission of Priority Documents (with copies of priority documents)

::ODMA\MHODMA\CB;234636;1

Appendix A

Marked-Up Version of Amended Claims

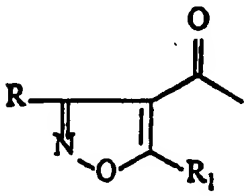
8. (Amended) A method according to claim 6 in which an encapsulated isoxazole is used, comprising [isoxazole derivative] an isoxazole compound of the general formula I



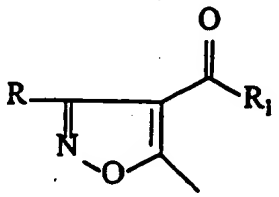
(I)

wherein:

A represents a group (A-1) or (A-2):



(A-1)



(A-2)

wherein:

R represents a hydrogen atom or a halogen atom; a straight- or branched-chain alkyl or alkenyl or alkynyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms; a cycloalkyl group containing from 3 to 6 carbon atoms optionally substituted by one or more groups R^5, one or more halogen atoms or a group $-CO_2R^3$; or a group selected from $-CO_2R^3$, $-COR^5$, cyano, nitro, $-CONR^3R^4$ and $-S(O)_kR^{13}$;

R^1 represents a straight- or branched-chain alkyl, alkenyl or alkynyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms, or a cycloalkyl group containing from three to six carbon atoms optionally substituted by one or more groups R^5 or one or more halogen atoms;

R^2 represents a halogen atom; a straight- or branched-chain alkyl, alkenyl or alkynyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms; a straight- or branched-chain alkyl group containing up to six carbon atoms which is substituted by one or more groups $-OR^5$; or a group selected from nitro, cyano, $-CO_2R^5$, $-S(O)_pR^6$, $-O(CH_2)_mOR^5$, $-COR^5$, $-NR^{11}R^{12}$, $-N(R^8)SO_2R^7$, $-N(R^8)CO_2R^7$, $-OR^5$, $-OSO_2R^7$, $-SO_2NR^3R^4$, $-CONR^3R^4$, $-CSNR^3R^4$, $-(CR^9R^{10})_t-S(O)_qR^7$ and $-SF_5$; or two groups R^2, on adjacent carbon atoms of the phenyl ring may, together with the carbon atoms to which they are attached, form a 5 to 7 membered saturated or unsaturated heterocyclic ring containing up to three ring heteroatoms selected from nitrogen, oxygen and sulfur, which ring is optionally substituted by one or more groups selected from halogen, nitro, $-S(O)_pR^{13}$, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, =O (or a 5- or 6-membered cyclic acetal thereof), and $=NO-R^3$, it being understood that a sulphur atom, where present in the ring, may be in the form of a group -SO- or $-SO_2-$;

n represents an integer from one to five; when n is greater than one the groups R^2 may be the same or different;

R^3 and R^4 each independently represent a hydrogen atom, or a straight- or branched-chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms;

R^5 represents a straight- or branched-chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms; or a straight- or branched-chain alkenyl

or alkynyl group containing from two to six carbon atoms which is optionally substituted by one or more halogen atoms;

R^6 and R^7, which may be the same or different, each represent R^5 or phenyl optionally substituted by from one to five groups which may be the same or different selected from a halogen atom, a straight- or branched-chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms, nitro, cyano, $-CO_2R^5$, $-S(O)_pR^{13}$, $-NR^{11}NR^{12}$, $-OR^5$, and $-CONR^3R^4$;

R^8, R^9 and R^{10} each represent a hydrogen atom or R^6;

R^{11} and R^{12} each represent hydrogen or R^5;

R^{13} represents a straight- or branched-chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms;

k, p and q independently represent the values zero, one or two;

m represents one, two or three;

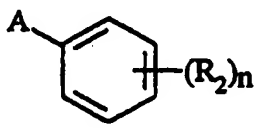
t represents an integer from one to four; when t is greater than one, the groups R^9 and R^{10} may be the same or different;

or an agriculturally acceptable salt or metal complex thereof;

encapsulated with a solid film comprising an inert material itself having no substantial herbicidal activity.

9. (Twice Amended) A method according to claim 8 in which the isoxazole [derivative] compound is in the form of granules of from 0.1 to 50 μm in size.

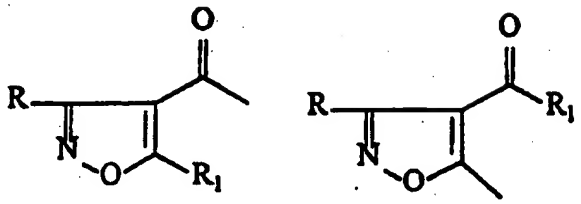
10. (Twice Amended) A method according to claim 1 in which the isoxazole [derivative] herbicide is a compound [is] of general formula I :



(I)

wherein:

A represents a group (A-1) or (A-2):



(A-1) (A-2)

wherein:

R represents a hydrogen atom or a halogen atom; a straight- or branched-chain alkyl or alkenyl or alkynyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms; a cycloalkyl group containing from 3 to 6 carbon atoms optionally substituted by one or more groups R^5, one or more halogen atoms or a group $-CO_2R^3$; or a group selected from $-CO_2R^3$, $-COR^5$, cyano, nitro, $-CONR^3R^4$ and $-S(O)_kR^{13}$;

R^1 represents a straight- or branched-chain alkyl, alkenyl or alkynyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms, or a cycloalkyl group containing from three to six carbon atoms optionally substituted by one or more groups R^5 or one or more halogen atoms;

R^2 represents a halogen atom; a straight- or branched-chain alkyl, alkenyl or alkynyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms; a straight- or branched-chain alkyl group containing up to six carbon atoms which is substituted by one or more groups $-OR^5$; or a group selected from nitro, cyano, $-CO_2R^5$, $-S(O)_pR^6$, $-O(CH_2)_mOR^5$, $-COR^5$, $-NR^{11}R^{12}$, $-N(R^8)SO_2R^7$, $-N(R^8)CO_2R^7$, $-OR^5$, $-OSO_2R^7$, $-SO_2NR^3R^4$, $-CONR^3R^4$, $-CSNR^3R^4$, $-(CR^9R^{10})_t$-$S(O)_qR^7$ and $-SF_5$; or two groups R^2, on adjacent carbon atoms of the phenyl ring may, together with the carbon atoms to which they are attached, form a 5 to 7 membered saturated or

unsaturated heterocyclic ring containing up to three ring heteroatoms selected from nitrogen, oxygen and sulfur, which ring is optionally substituted by one or more groups selected from halogen, nitro, $-S(O)_pR^{13}$, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, =O (or a 5- or 6-membered cyclic acetal thereof), and $=NO-R^3$, it being understood that a sulphur atom, where present in the ring, may be in the form of a group -SO- or $-SO_2-$;

n represents an integer from one to five; when n is greater than one the groups R^2 may be the same or different;

R^3 and R^4 each independently represent a hydrogen atom, or a straight- or branched-chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms;

R^5 represents a straight- or branched-chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms; or a straight- or branched-chain alkenyl or alkynyl group containing from two to six carbon atoms which is optionally substituted by one or more halogen atoms;

R^6 and R^7, which may be the same or different, each represent R^5 or phenyl optionally substituted by from one to five groups which may be the same or different selected from a halogen atom, a straight- or branched-chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms, nitro, cyano, $-CO_2R^5$, $-S(O)_pR^{13}$, $-NR^{11}NR^{12}$, $-OR^5$, and $-CONR^3R^4$;

R^8, R^9 and R^{10} each represent a hydrogen atom or R^6;

R^{11} and R^{12} each represent hydrogen or R^5;

R^{13} represents a straight- or branched-chain alkyl group containing up to six carbon atoms which is optionally substituted by one or more halogen atoms;

k, p and q independently represent the values zero, one or two;

m represents one, two or three;

t represents an integer from one to four; when t is greater than one, the groups R^9 and R^{10} may be the same or different;

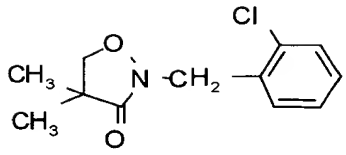
or an agriculturally acceptable salt or metal complex thereof.

Appendix

clomazone (159)

Herbicide

HRAC F_3 **WSSA** 13; isoxazolidinone



NOMENCLATURE

Common name clomazone (BSI, ANSI, draft E-ISO, (*f*) draft F-ISO)
IUPAC name 2-(2-chlorobenzyl)-4,4-dimethyl-1,2-oxazolidin-3-one; 2-(2-chlorobenzyl)-4,4-dimethylisoxazolidin-3-one
Chemical Abstracts name 2-[(2-chlorophenyl)methyl]-4,4-dimethyl-3-isoxazolidinone
Other names dimethazone* **CAS RN** *[81777-89-1]* **Development codes** FMC 57 020

PHYSICAL CHEMISTRY

Mol. wt. 239.7 **M.f.** $C_{12}H_{14}ClNO_2$ **Form** Clear, colourless to light brown, viscous liquid. **M.p.** 25 °C **B.p.** 275 °C **V.p.** 19.2 mPa (25 °C) K_{ow} logP = 2.5 **Henry** 4.19×10^{-3} Pa m^3 mol^{-1} **S.g./density** 1.192 (20 °C) **Solubility** In water 1.1 g/l. Miscible with acetone, acetonitrile, chloroform, cyclohexanone, dichloromethane, methanol, toluene, heptane, dimethylformamide. **Stability** Stable at ambient temperatures for at least 2 y; stable at 50 °C for at least 3 mo. In sunlight, DT_{50} >30 d in aqueous solution. **F.p.** 70-75 °C (closed cup)

COMMERCIALISATION

History Herbicide introduced by FMC Corp. **Patents** US 4405357 **Manufacturers** FMC

APPLICATIONS

Biochemistry Inhibits carotenoid biosynthesis; target enzyme not known. **Mode of action** Selective herbicide, absorbed by the roots and shoots and translocated upward. Susceptible species emerge but are devoid of pigmentation. **Uses** Control of broad-leaved and grass weeds in soya beans, peas, maize, oilseed rape, sugar cane, cassava, pumpkins, and tobacco. Applied pre-emergence or pre-plant incorporated. **Phytotoxicity** Foliar contact or vapours may cause visual symptoms of chlorosis to nearby sensitive plants. **Formulation types** CS; EC; WP. **Compatibility** Compatible with many other herbicides, e.g. metribuzin, linuron, chloramben, alachlor, trifluralin, pendimethalin, metolachlor, oryzalin or ethalfluralin. **Selected tradenames:**

'Command' (FMC); **mixtures:** 'Commence' (+ trifluralin) (FMC); 'Brasan' (+ dimethachlor) (Syngenta); 'Cozor Trio' (+ dimethachlor+ napropamide) (Syngenta)

OTHER TRADENAMES
'Centium' (FMC); 'Cirrus' (FMC); 'Gamit' (FMC) **mixtures:** 'Authority One-Pass' (+ sulfentrazone) (FMC); 'Command Cotton' (+ fluometuron) (FMC); 'Galaxy' (+ pendimethalin) (FMC); 'RiceMax' (+ propanil) (FMC); 'Centaure' (+ linuron+ trifluralin) (Dow AgroSciences); 'Nimbus' (+ metazachlor) (BASF)

ANALYSIS
Product by gc with FID or hplc with u.v. detection. Details and **residue** methods reviewed (A. W. Chen in *Comp. Anal. Profiles,* Chapt. 6).

MAMMALIAN TOXICOLOGY
Oral Acute oral LD_{50} for male rats 2077, female rats 1369 mg/kg. **Skin and eye** Acute percutaneous LD_{50} for rabbits >2000 mg/kg. Practically non-irritating to eyes (rabbits). **Inhalation** LC_{50} (4 h) for rats 4.8 mg/l. **NOEL** (2 y) for rats 4.3 mg/kg daily. **ADI** 0.043 mg/kg (proposed). **Toxicity class** WHO (a.i.) II; EPA (formulation) III

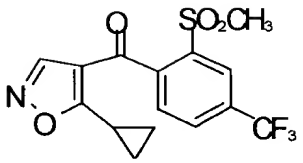
ECOTOXICOLOGY
Birds Acute oral LD_{50} for bobwhite quail and mallard ducks >2510 mg/kg. LC_{50} (8 d) for bobwhite quail and mallard ducks >5620 ppm. **Fish** LC_{50} (96 h) for bluegill sunfish 34, Atlantic silverside 6.26, rainbow trout 19 mg/l. **Daphnia** LC_{50} (48 h) 5.2 mg/l. **Algae** EC_{50} (48 h) 2.10 mg/l. **Other aquatic spp.** LC_{50} for pink shrimp 8.9, eastern oyster 5.3 mg/l. **Worms** LC_{50} (14 d) for *Eisenia foetida* 156 mg/kg.

ENVIRONMENTAL FATE
Soil/Environment DT_{50} in soil *c.* 30-135 d. K_{oc} 150-562, suggesting clomazone would be mobile in soil; however, in field trials it was found not to leach beyond the top 10 cm of soil (J. Rosenwald *et al.*, *Proc. 9th IUPAC Int. Congr. Pestic. Chem.*, London, 1998, 6A-006).

isoxaflutole (467)

Herbicide

HRAC F_2 **WSSA** 28; isoxazole



NOMENCLATURE

Common name isoxaflutole (BSI, pa ISO)

IUPAC name 5-cyclopropyl-1,2-oxazol-4-yl α,α,α-trifluoro-2-mesyl-*p*-tolyl ketone

Chemical Abstracts name (5-cyclopropyl-4-isoxazolyl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl]methanone

CAS RN *[141112-29-0]* **Development codes** RPA 201772 (Rhône-Poulenc)

PHYSICAL CHEMISTRY

Composition Tech. is *c.* 98% pure. **Mol. wt.** 359.3 **M.f.** $C_{15}H_{12}F_3NO_4S$ **Form** Off-white or pale yellow solid. **M.p.** 140 °C **V.p.** 1×10^{-3} mPa (25 °C) K_{ow} logP = 2.32 **Henry** 1.87×10^{-5} Pa m^3 mol^{-1} (20 °C) **S.g./density** 1.590 **Solubility** In water 6.2 mg/l (pH 5.5, 20 °C). **Stability** Stable to heat (14 d at 54 °C) and to light. DT_{50} in water 1 d at pH 7.

COMMERCIALISATION

History Under development from 1992. Reported by B. M. Luscombe *et al.* (*Proc. Br. Crop Prot. Conf. - Weeds,* 1995, **1**,35). **Patents** EP 0527036 **Manufacturers** Aventis

APPLICATIONS

Biochemistry Rapidly metabolised in plants, and in the soil, by opening of the isoxazole ring, to form a diketonitrile, which is the active species (K. E. Pallett *et al.*, *Pest Manag. Sci.* **57**, 133 (2001) and refs. therein); this is a *p*-hydroxyphenyl pyruvate dioxygenase inhibitor. This enzyme converts *p*-hydroxyphenyl pyruvate to homogentisate, a key step in plastoquinone biosynthesis. Inhibition leads to indirect inhibition of carotenoid biosynthesis, giving rise to chlorosis of new growth. **Mode of action** Systemic by either root or foliar uptake. **Uses** Broad-spectrum grass and broad-leaved weed control in maize and sugar cane. Applied at 75-140 g/ha pre-emergence or pre-plant; the spectrum can be enhanced by mixture with other active ingredients. **Formulation types** SC; WG; WP. **Selected tradenames:** 'Balance' (Aventis); 'Merlin' (Aventis)

OTHER TRADENAMES

'Alliance' (Aventis); 'Converge' (Aventis); 'Provence' (Aventis) **mixtures:** 'Acajou' (+ aclonifen) (Aventis); 'Atoll' (+ atrazine) (Aventis); 'Lagon' (+ aclonifen) (Aventis); 'Cadou Star' (+ flufenacet) (Bayer); 'Epic' (+ flufenacet) (Bayer)

ANALYSIS
By hplc with u.v. detection.

MAMMALIAN TOXICOLOGY
Oral Acute oral LD_{50} for rats >5000 mg/kg. **Skin and eye** Acute percutaneous LD_{50} for rabbits >2000 mg/kg. Not a skin irritant; minimal eye irritation (rabbits). Not a skin sensitiser. **Inhalation** LC_{50} (4 h) for rats >5.23 mg/l. **NOEL** (2 y) for rats 2 mg/kg daily. **Other** Non-mutagenic, non-neurotoxic. **Toxicity class** EPA (formulation) III

ECOTOXICOLOGY
Birds Acute oral LD_{50} (14 d) for quail and mallard ducks >2150 mg/kg; dietary LC_{50}(8 d) >5000 ppm. **Fish** Non-toxic at limit of water solubility. **Daphnia** Non-toxic at limit of water solubility. **Algae** EC_{50} for *Selenastrum capricornutum* 0.016 mg/l. **Other aquatic spp.** EC_{50} (96 h) for Eastern oyster (*Crassostrea virginica*) 3.4 mg/l, mysid shrimp (*Mysidopsis bahia*) 18 µg/l. **Bees** LD_{50} (oral and contact) >100 µg/bee. **Worms** Non-toxic at 1000 mg/kg.

ENVIRONMENTAL FATE
Animals Following oral administration, isoxaflutole is rapidly excreted. **Plants** Plant metabolism study demonstrated that residue levels at harvest are very low, and comprise mainly a non-toxic metabolite. **Soil/Environment** In laboratory soil studies, degradation proceeds via hydrolysis and microbial degradation, with final mineralisation to CO_2. Isoxaflutole and its major metabolites are potentially mobile in soil under simulated high rainfall; however field studies indicate that residues remain in the surface horizons; after 4 months, virtually no residues remain in the soil.